

Assessing the Renal Toxicity of Depleted Uranium and Other Uranium Compounds

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1991 Persian Gulf War – Combat Use of DU Munitions



M1 Abrams



AV-8B Harrier II



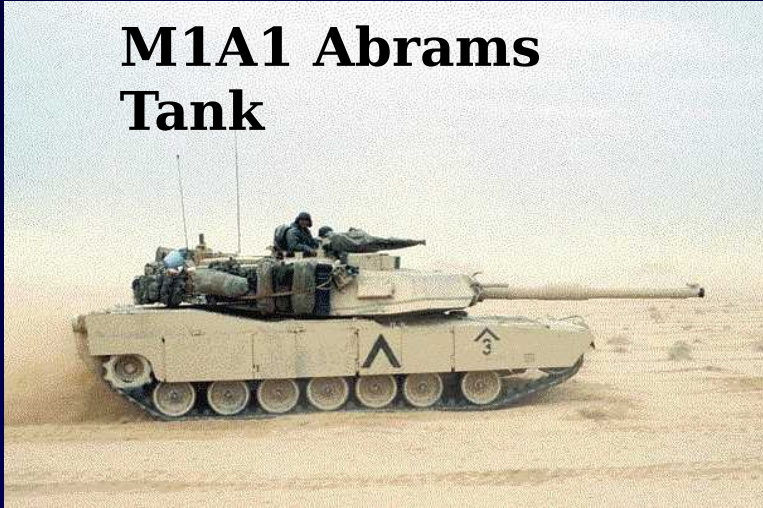
M60 tank



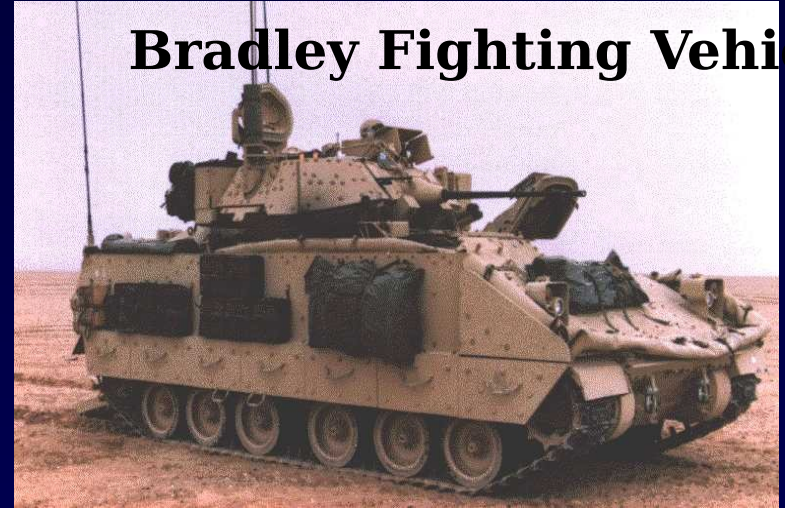
A-10 Thunderbolt

1991 Gulf War: U.S. Vehicles involved in Fratricide Incidents

**M1A1 Abrams
Tank**



Bradley Fighting Vehicle



- 21 U.S. Combat Vehicles struck by DU munitions during 1991 Persian Gulf War
- Estimated 113 soldiers as casualties
- 30-60 individuals provided assistance after impact (First Responders)

Other Sources & Uses of Uranium

- Mining
- Milling (refinement)
- Nuclear reactors
- Aircraft counterweights
- Semi-conductors (? Research ongoing)

DU Internalization

- Inhalation

- Particles <10 microns are respirable
- Soluble forms absorbed, distributed to other organs
- Less soluble forms removed slowly

- Ingestion

- Absorption from gut is inefficient ($\leq 2.0\%$)

- Wounds

- Particles may enter through open wounds

- Embedded fragments

- Solubilize and distribute

Potential Target Organs

- **Kidney**
- Lung
- Lymph nodes
- Skeleton
- Brain
- Reproductive

Chemical Guidelines for Uranium

- ACGIH, OSHA & NIOSH STEL
 - 0.6 mg/m³
- AIHA ERPG's
 - 10 – 50 mg/m³
- DOE TEEL
 - 0.05 – 10 mg/m³
- ANSI thresholds for renal damage
 - 4 mg inhalation
- ICRP
 - 3 µg U /g kidney

ANSI Guidelines

Health Effects	Uranium intake by 70 kg person (mg)
50% lethality	230
Permanent renal damage	40
Transient renal injury or effect	8
No effect	4

ICRP Guideline- 3 $\mu\text{g U /g}$ kidney

- Based on extrapolation of radiological limit from ICRP Publication 2 (Spoor & Hursh, 1973)

$$\frac{5 \times 10^{-3}}{0.33 \times 10^{-6}} \times \frac{0.065}{300} = 3.2 \mu\text{g/g}$$

$5 \times 10^{-3} \mu\text{Ci} = "q";$ permissible whole body content

0.33×10^{-6} = specific activity of natural uranium

0.065 = kidney fraction of q

300g = kidney mass for Standard Man

ICRP Guideline- 3 $\mu\text{g U /g}$ kidney

- Extrapolation from radiological limit was in agreement with animal data (Voegtlin & Hodge, 1953)
 - 4 mammalian species
 - 200 $\mu\text{g U/m}^3$
 - ~40 hours/week up to 1 year
 - Average kidney burdens 0.1 $\mu\text{g/g}$ – 2.7 $\mu\text{g/g}$
 - Mild tubular injury after 1 year

Problem:

Predicting an effect based on kidney burden of uranium.



Solution:

Develop a model based on documented effects and kidney burdens



Acute Human Exposures to Uranium

Intake Route (n)	Chemical Form	Intake (mg U)	Peak µg U/g kidney	Effect	Reference
Ingestion	Acetate	8500	100	+++	Pavlakakis et al. 1996
Dermal	Nitrate	130	35	+++	Zhao and Zhao 1990
Inhalation	Tetrafluoride	920	10	++	Zhao and Zhao 1990
Injection (2)	Nitrate	11 - 16	4 - 6	+	Luessenhop et al. 1958
Dermal	Nitrate	10	3	++	Butterworth 1955
Inhalation	Hexafluoride	24	2.5	+	Fisher et al. 1990a
Injection	Nitrate	5.9	2	+	Luessenhop et al. 1958
		5.5	2	-	
		4.3	1.5	-	
Inhalation (3)	Hexafluoride	40-50	1.2 - 4	+	Kathren and Moore 1986
Inhalation (7)	Hexafluoride	11 - 18	1.1 - 1.9	-	Fisher et al. 1990a
Ingestion	Nitrate	470	1	+	Butterworth 1955
Inhalation	Hexafluoride	20	1	-	Boback 1975
Inhalation (5)	Hexafluoride	6 - 8.7	0.62 - 0.9	-	Fisher et al. 1990a

Classification of Renal Symptoms

Clinical symptoms of renal dysfunction	
Severe	+++
Biochemical indicators of Renal dysfunction	
Protracted	++
Transient	+
Negative	-

Renal Effects Groups

Renal Effects Group	Number of Cases	µg U/ g Kidney Range
0 (-)	15	0.62 - 2
1 (+)	8	1 - 6
2 (++)	2	3 - 10
3 (+++)	2	35 - 100

Risk Model to Predict Effects Groups

- Discriminant analysis used
- Based on log-transformed data
- Discriminant function based on linear combination of
 - Predictor variable
 - $\mu\text{g U/g kidney}$
- Correctly identified 85.2% of cases

Discriminant Function

$$D = 4.378 \times \text{Log } (\mu\text{g U/g kidney}) - 1.519$$

Renal Effects Groups

Effects Group	Effects	D (range)	µg U/g kidney
0	No effect	≤ 0.0	≤ 2.2
1	Transient	$> 0.0 - 2.0$	$> 2.2 - 6.4$
2	Protracted	$> 2.0 - 4.0$	$> 6.4 - 18$
3	Severe	> 4.0	> 18

Calculated Kidney Concentration, 2000 HRA

Estimated Kidney Concentration (μg U/g)*	Effects Group
1.5 (upper bound)	0
0.2 (lower bound)	0

*based on a single shot

Capstone DU Aerosol Study, Updated HRA

- Testing of aerosols generated by perforation of armored vehicles with DU penetrators
- Firing at ballistic turrets and hulls
- Characterizing chemical concentration and composition over first 2 hours
- Predicted intakes based on assumption that
 - ventilation systems off
 - no PPE

Risk Model

- Can be used to predict risk to soldiers
- Can be used for other acute exposures to uranium compounds
- Can be used to assess risk of other compounds

Predicting Risk to Soldiers

RES 0	No exposure
RES 1	Some exposure (negligible risk)
RES 2	75 rad < 125 rad (Moderate risk)
RES 3	> 125 rad (Emergency risk)

Issues

- Small N (=2 Groups 2, 3)
- May not apply to longer than acute exposures
- **Needs to be validated in an animal model**

QUESTIONS?